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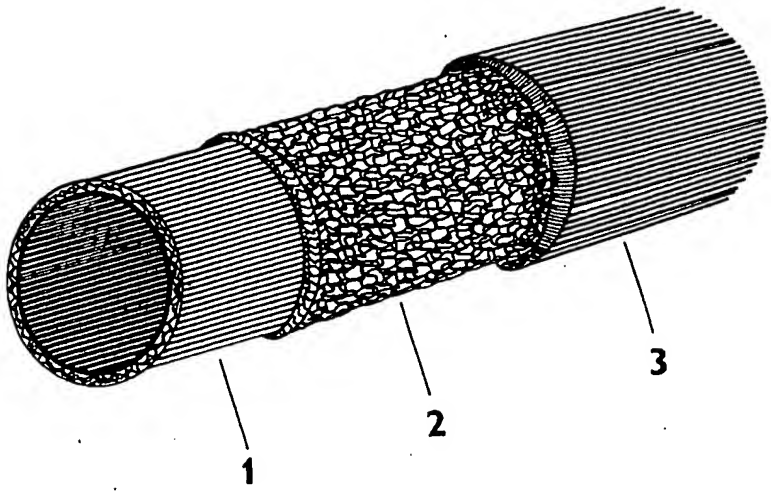
(54) Three-layer vascular prosthesis.

(57) The invention relates to three-layer vascular prostheses comprising an internal layer 1, a middle layer 2 and an external layer 3 which is characterized in that the middle layer 2 is made from a physiologically non-resorbable, porous material, and the internal layer 1 and the external layer 3 are self-supporting and are made from a physiologically resorbable, fibrillar material, and are tanned. The internal layer 1 and the external layer 3 preferably consist of collagen, but have different resorbability. The middle layer 2 is preferably made from inert fibres, preferably synthetic fibres, by means of textile technology.

The biologically resorbable layers preferably comprise chemically or physically bonded or incorporated pharmacologically active substances.



The present invention relates to three-layer vascular prostheses, essentially consisting of an internal layer, a middle layer and an external layer, and particularly being in the form of a tube,and a method for manufacturing these prostheses. The prostheses according to the invention are particularly advantageous for the reconstruction of vessels of small diameter and with a low flow.

Vascular prostheses on the basis of synthetic fibres manufactured by means of textile technology have already been known. They differ from each other by their construction, the materials used and eventually also by the manufacturing technology. The goal of these different approaches according to the prior art is to improve the short- and long-term patency of the reconstruction, to improve the surgical characteristics, and to overcome some negative effects, such as for example provocation of infections. There have already been known combined vascular prostheses comprising non-resorbable materials, for example synthetic fibres, and resorbable materials, for example catgut, gelatine, collagen, albumin, etc. These resorbable materials are usually introduced by means of impregnation.

CS-A-116 540 relates to highly porous collagen-fabric vascular prostheses and a method for the manufacturing thereof. In these prior art prostheses, a combination of a self-supporting tube made from collagen with a knitted frame made from synthetic fibres serving for a substantial increase of the porosity of the fabric is used. A similar solution has been known from CH-A-645 532 which describes a vascular prosthesis of tubular form, where an internal layer, which is porous and made from a resorbable material, is provided on the internal surface of an external layer manufactered from a non-resorbable material. A fundamentally opposite construction of a vascular prosthesis has been known from FR-A-2 541 888. The principal disadvantages of both these solutions on the basis of a two-layer structure in comparison with the present invention, which is based on a three-layer structure, are the not completely secured attachement of the layers and the not exactly defined resorbability of the resorbable layer.

EP-A-47 231 relates to a three-layer vascular prosthesis. However, all the three layers of this prosthesis are made from a non-resorbable material, the external layer comprises interstices produced by means of a laser beam, and the middle layer is a knitted fabric. The principal disadvantages of this construction are the non-resorbability of all layers and the high costs of the laser processing of the external layer.

It is the object of the present invention to overcome the problems of the prior art prostheses and to provide vascular prostheses and methods for the manufacturing thereof which effectively prevent leaking around the sutures and simultaneously positively influence the character of the newly formed tissue surrounding the vascular prosthesis. In addition thereto, their structure should guarantee the temporary attachment of all layers together during the time needed for the surgical implantation. Furthermore, the vascular prostheses should be obtainable by a simple and low cost process.

The above object is achieved according to the claims. The dependent claims relate to preferred embodiments.

The three-layer vascular prostheses according to the present invention comprise an internal layer, a middle layer and an external layer and are characterized in that the middle layer is made from a physiological non-resorbable, porous material, and the internal layer and the external layer are self-supporting and are made from a physiologically resorbable fibrillar material, and are tanned.

The non-resorbable material is preferably made of synthetic fibres. The internal layer as well as the external layer are preferably made from collagen, preferably bovine collagen.

The middle layer is preferably a porous fabric manufactured by means of textile technology and made of biologically inert fibres, preferably synthetic fibres.

The resorbability of the internal layer which has been influenced by the tanning is preferably such that the resorption is completed 2 to 3 months after the implantation into the organism.

The self-supporting internal layer of the prostheses which is preferably a tube, may be used as it is, or a pharmacologically active agent, preferably heparin, acetylsalicylic acid, prostaglandin, etc. is chemically or physically bonded to or incorporated into the material of the internal layer.

The external layer has also a self-supporting structure and is made from a resorbable, fibrillar material, for example collagen. The resorbability of the external layer which is influenced by the tanning is made such that its resorption is completed 3 to 6 weeks after the implantation into the organism. The external layer of the prostheses, which is preferably in the form of a tube, may also be used as it is, or it may comprise a pharmacologically active agent, preferably fibronectin and/or antibiotics, etc., which are chemically or physically bonded to or incorporated into the material of the external layer.

The middle layer which is manufactered by means of textile technology from non-resorbable, biologically inert fibres is the only layer of this prosthesis which permanently remains in the organism and thus forms the mechanical support for the newly formed vascular wall produced in the course of the healing processes in the organism.

The internal layer, which has a resorption time

between 2 and 3 months, first prevents leakage of blood through the porous fabric, and secondly prevents seeding of thrombocytes because of its perfect smoothness and eventually also by the effect of the pharmacologically active agents, such as heparin, which improves the conditions for the immediate postoperative patency even in cases of reconstructions which are problematic in view of the high flow.

The external resorbable layer, which has a shorter resorption time, which is adjusted by the tanning procedure, meets three requirements. At first, its chemical composition allows to keep all three layers temporarily together to form one entire structure, which is basically important for the possibility of a surgical implantation. Secondly, this layer has a higher swelling capacity due to the chemical tanning treatment, which allows a faster resorption and leads to a rapid closure around the holes made by the surgical needle and the suture material used for making the surgical connections; this way, bleeding around the stitches, which is an unpleasant und undesired characteristic of prior art prostheses, is effectively prevented. Thirdly, the optional incorporation of pharmacologically active substances, such as fibronectin or antibiotics, allows to intentionally influence the quality of the tissues newly formed around the prostheses as the result of the healing capacity of the organism.

In comparison with known prostheses, the three-layer prostheses according to the present invention are highly advantageous, particularly from the surgical point of view, in particular because they prevent bleeding around stitches, and, on the other hand, from the biologically point of view, because the character of the newly formed tissues surrounding the vascular prostheses may be intentionally influenced. It is also to be noted that the temporary connection of the three layers to form one single, entire structure for the time of surgical implantation is substantially more perfect than in prior art multi-structure prostheses.

In the following, the invention will be further explained with more details by way of examples with reference to the accompanying drawing.

The drawing is a schematical axonometric view of a three-layer vascular prosthesis in accordance with the present invention.

The self-supporting internal layer 1 is made from a resorbable fibrillar material, for example collagen; the same applies for the self-supporting external layer 3. The internal layer 1 as well as the external layer 3 are tanned. For that reason, as long as their structure is not impaired by the postoperative resorption process, they are self-supporting. The middle layer 2 is made from a non-resorbable material, preferably manufactured by means of textile technology, and consisting of biologically inert synthetic fibres, and by itself being elastic and pliable.

The prosthesis preferably has tubular form, as is shown in the drawing.

According to an advantageous example of the manufacturing method, the internal layer 1 is made from bovine collagen in the form of a self-supporting tube of the desired length and diameter. This internal layer 1 is then tanned by means of a biologically acceptable tanning agent, for example by means of glutardialdehyde or trimethyltriaminotriazin or thriethyltriaminotriazin. The temperature for the tanning is preferably kept within the range of 50 to 70 °C. By the tanning process, the swelling capacity is reduced. For example, the swelling capacity in 0.9 % NaCl solution is decreased to 40 to 50 %.

After the internal layer 1 has been dried, the middle layer 2 made of the non-resorbable porous material and manufactured by means of textile technology is applied thereon. The middle layer 2 is made of biologically inert fibres, advantageously synthetic fibres, for example from biologically inert polyester fibres. After the application of the middle layer 2, the self-supporting external layer 3 of corresponding diameter is applied onto the middle layer 2. The external layer 3 is preferably made from bovine collagen. According to a preferred embodiment, the external layer 3 provided on the non-resorbable porous middle layer 2 is then tanned by means of a biologically acceptable tanning agent, for example glutardialdehyde, trimethyltriaminotriazin or triethyltriaminotriazin. The tanning is preferably carried out at a temperature within the range from 45 to 58 °C. By this tanning process, the swelling capacity is reduced, preferably to such an extent that the swelling capacity in 0.9 % NaCl solution is between 70 and 100 %. The thus obtained prosthesis is finally sterilized, preferably by gamma-irradiation at a irradiation dosis of 2.5 to 2.8 megarad.

According to another advantageous example, the self-supporting internal layer 1 is also made from bovine collagen, however, prior to manufacturing the internal layer 1, heparin is incorporated in a concentration of 5000 to 30000 international units per 1000 g. The further process corresponds to the above-described procedure.

In accordance with another advantageous embodiment, the internal layer 1 and the middle layer 2 are made in the manner described above, however, before the external layer 3 is provided on the middle layer 2, fibronectin is incorporated into the material of the external layer 3 in a concentration of 5 to 10 mg/g of dry collagen.

According to another preferred embodiment, a reinforcing spiral made from a solid, biologically inert liner is provided between the middle layer 2

and the external layer 3. The diameter preferably corresponds to the total diameter of the vascular prosthesis. This liner may be made for example from polytetrafluoroethylene or a polyester.

Such a reinforcing spiral may also be provided on the outer surface of the external layer 3.

It is further advantageous according to the present invention to make the three layers of the prosthesis in the form of a truncated cone, where it is specifically preferred that the end diameters of each of the tubes differ by at least 20 %. It is further advantageous to provide a visible mark of the longitudinal axis on or in the middle layer 2.

In accordance with a further preferred embodiment, the material of the internal layer 1 and/or of the external layer 3 comprises an aqueous solution of glycerol in a concentration of 5 to 30 % by mass.

Claims

1. Three-layer vascular prostheses, comprising an internal layer (1), a middle layer (2) and an external layer (3), characterized in that the middle layer (2) is made from a physiologically non-resorbable porous material, and the internal layer (1) and the external layer (3) are self-supporting and are made from a physiologically resorbable fibrillar material, and are tanned.

2. The prostheses according to claim 1, characterized in that they are in the form of tubes.

3. The prostheses according to claim 1 or 2, characterized in that the non-resorbable porous material of the middle layer (2) consists of synthetic fibres, preferably physiologically inert polyester fibres, and preferably being made by means of textile technology.

4. The prostheses according to one of claims 1 to 3, characterized in that the internal layer (1) and/or the external layer (3) consist of collagen, preferably bovine collagen.

5. The prostheses according to one of claims 1 to 4, characterized in that the internal layer (1) is tanned to such an extent that its resorption is completed 2 to 3 months after implantation, and/or the external layer (3) is tanned to such an extent that its resorption is completed 3 to 6 weeks after implantation.

6. The prostheses according to one of claims 1 to 5,

characterized in that

a pharmacologically active agent, preferably heparin, acetylsalicylic acid and/or prostaglandin, is chemically or physically bonded to or incorporated into the material of the internal layer (1),

and/or

a pharmacologically active agent, preferably fibronectin and/or antibiotics, is chemically or physically bonded to or incorporated into the material of the external layer (3).

7. The prostheses according to one of claims 1 to 6, characterized in that the material of the internal layer (1) and/or the material of the external layer (3) comprises an aqueous solution of glycerol in a concentration of 5 to 30 % by mass.

8. The prostheses according to one of claims 1 to 7, characterized in that they comprise

a reinforcing spiral made of a solid, biologically inert liner, preferably made of polytetrafluoroethylene or a polyester, provided between the middle layer (2) and the external layer (3), the diameter of the liner preferably corresponding to the total diameter of the prosthesis, and/or

a reinforcing spiral made of a solid, biological inert liner, preferably made of polytetrafluoroethylene or a polyester, provided on the outer surface of the external layer (3).

9. The prosthesis according to one of claims 1 to 8, characterized in that the internal layer (1), the middle layer (2) and the external layer (3) have the form of a truncated cone tube, the end diameters of each of the tubes preferably differing by at least 20 %.

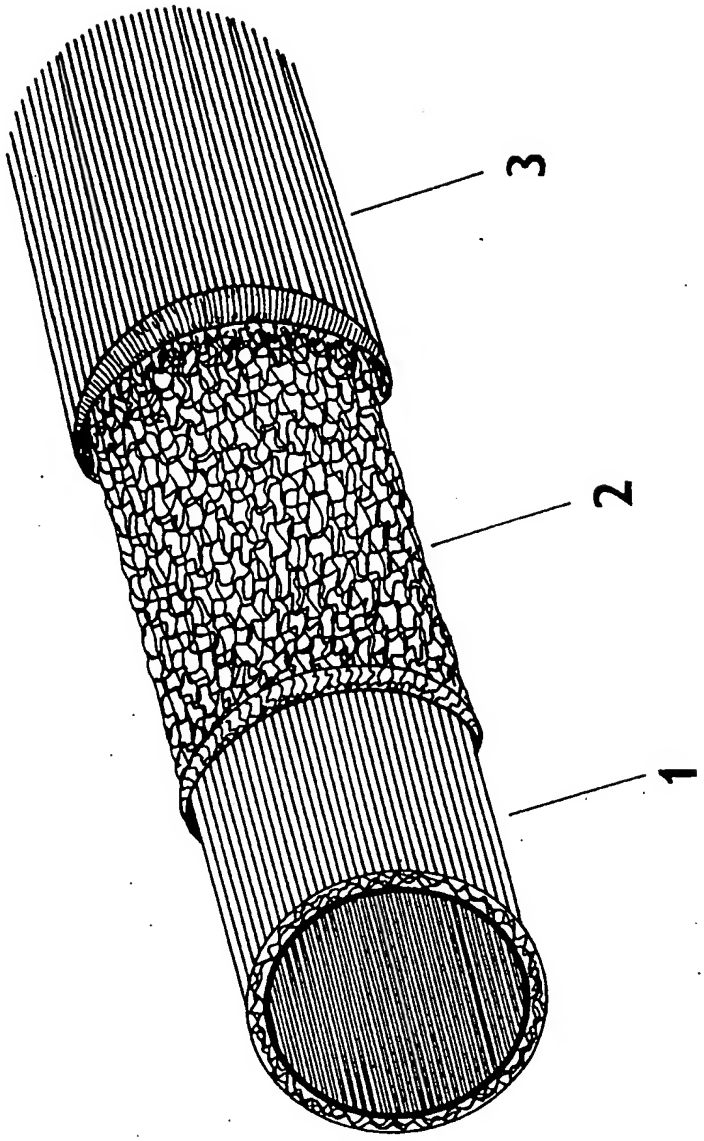
10. The prostheses according to one of claims 1 to 9, characterized in that the middle layer (2) comprises a visible mark of the longitudinal axis.

11. A method for manufacturing the prostheses according to claims 1 to 10, comprising the following steps:
    (A) Preparing a self-supporting internal layer (1) from a physiologically resorbable fibrillar material, preferably made from collagen, and more preferably made from bovine collagen,
    (B) tanning the internal layer (1) by means

of a biologically acceptable tanning agent, preferably glutaraldehyde, trimethylaminotriazin or triethylaminotriazin, to reduce the swelling capacity, preferably at a temperature of 50 to 70 °C,
(C) providing a middle layer (2) by applying a layer of a physiologically non-resorbable, porous material, preferably of physiologically inert fibres and more preferably of synthetic fibres, onto the internal layer (1),
(D) providing an external layer (3) by applying a self-supporting layer of a physiologically resorbable fibrillar material, preferably made from collagen, and more preferably made from bovine collagen, onto the middle layer (2),

and
(E) tanning the external layer (3) by means of a biologically acceptable tanning agent, preferably glutaraldehyde, trimethylaminotriazin or triethylaminotriazin, to reduce the swelling capacity, preferably at a temperature of 45 to 58 °C.

12. The method according to claim 11, characterized by one or more or all of the following measures:
- Before step A, or after step A and before step B, or after step B and before step C, a pharmacologically active agent, preferably heparin, acetylsalicylic acid and/or prostaglandin, is chemically or physically bonded to or incorporated into the material of the internal layer (1),
- before the formation of the external layer (3) in step D, or after step D and before step E, or after step E, a pharmacologically active agent, preferably fibronectin and/or antibiotics, is chemically or physically bonded to or incorporated into the material of the external layer (3);
- in step C, fibres, a non-woven fabric or a textile web made of a physiologically inert polyester are used as non-resorbable porous material;
- an aqueous solution of glycerol is incorporated into the internal layer (1) and/or the external layer (3) in a concentration of 5 to 30 % by mass;
- a reinforcing spiral made of a solid, biologically inert liner, preferably made of polytetrafluoroethylene or a polyester, is provided between the middle layer (2) and the external layer (3) and/or on the outer surface of the external layer (3);
- the internal layer (1), the middle layer (2) and the external layer (3) are made such that they have the form of a truncated cone tube, the end diameters of each of the tubes preferably differing by at least 20 %;
- a visible mark of the longitudinal axis is provided in or on the middle layer (2).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EUROPEAN SEARCH REPORT

Application Number

EP 91 12 2196

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	FR-A-2 558 720 (MEADOX MEDICALS INC.) * claims 1-4,12,13; figure 1 *	1-7,11	A61F2/06
Y	EP-A-0 323 144 (VYZKUMNY USTAV POTRAVINARSKEHO PRUMYSLU) * column 1, line 45 - column 2, line 20 * * column 5, line 3 - line 27; figure 3 *	1-7,11	
A	US-A-4 319 363 (KETHARANATHAN) * claims 1-3; figure 1 *	1-5	
P,A	US-A-5 037 377 (ALONSO) * claims 1,2; figure 3 *	1-5	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A61F
A61L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	27 MARCH 1992	GODOT T.

CATEGORY OF CITED DOCUMENTS

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